# THE ROLE OF LEFT ATRIAL CHAMBER SIZE AS ASSESSED BY ECHOCARDIOGRAPHY IN DETERMINING THROMBOEMBOLIC COMPLICATIONS OF ATRIAL FIBRILLATION.

Cynthia Ann Hall

1986

# The Role of Left Atrial Chamber Size as Assessed by Echocardiography in Determining Thromboembolic Complications of Atrial Fibrillation.

A Thesis Submitted to the Yale University School of Medicine in Partial Fulfillment of the Requirements for the Degree of Doctor of Medicine

by

Cynthia Ann Hall

1986

ACKNOWLEDEMENTS

I would like to thank

Dr. Henry S. Cabin

Assistant Professor of Medicine

Cardiology Section

for much enthusiasm, encouragement and guidance.

ABSTRACT

The Role of Left Atrial Chamber Size
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To examine the usefulness of left atrial chamber size in predicting patients at risk for thromboembolic complications of atrial fibrillation without mitral stenosis, this study examined 176 patients having atrial fibrillation without mitral stenosis. All patients had left atrial chamber size measured by 2-D and M-Mode study. Clinical charts were reviewed for evidence of systemic embolization (central nervous system, mesenteric and peripheral). At the end of the study period, 25/116 (22%) patients with left atrial chamber size greater than or equal to 4.0cm as compared to 4/60(7%) patients with left atrial chamber size less than 4.0cm experienced a systemic embolism (p=.01). Therefore patients with atrial fibrillation without mitral stenosis and left atrial chamber size greater than or equal to 4.0cm

have a 3 time greater embolic frequency than patients with left atrial chamber size less than 4.0cm. Twenty-one of ninety-eight (21%) of patients with underlying organic heart disease embolized as compared to 8/78(10%) patients without heart disease who embolized ($p < .05$). Patients with chronic atrial fibrillation were more likely to embolize than those with paroxysmal atrial fibrillation. The risk of embolization was not confined to any discrete time period after the onset of atrial fibrillation.

TABLE OF CONTENTS

# INTRODUCTION

In the 1950's systemic embolization was shown to be a serious complication of atrial fibrillation when associated with mitral stenosis (1). Other researchers have since confirmed this finding (2,3,4). Because these thromboembolic events may have devastating consequences (5) efforts to prevent their occurrence are justified. Although other clinical entities associated with atrial fibrillation have been reported to increase the risk of embolization (2,3,4), the only widely accepted indication for anticoagulation in patients with atrial fibrillation is the presence of mitral stenosis. Unanswered questions regarding the efficacy, duration and risk of anticoagulation therapy have resulted in patients being untreated unless, the risk of embolization outweighed the risk of anticoagulation therapy. The incidence of spontaneous bleeding ranges from less than 1% to almost 10% on heparin therapy and complicates at least 5% of all courses of wafarin therapy, despite close regulation (10). Therefore, in this paper, patients with atrial fibrillation without mitral stenosis were reviewed to assess their overall risk of embolization and to identify any factors that could increase or decrease their risk. In particular, all patients underwent an echocardiogram to assess the influence of left atrial chamber size on embolic risk. This study showed that patients with atrial fibrillation without mitral stenosis and left atrial chamber size greater than or equal to 4.0cm were at three times greater risk for embolization than

those with left atrial size less than 4.0cm. Additionally, the presence of underlying heart disease, chronic atrial fibrillation and increased age significantly increased the embolic risk in the study population.

## Clinical Materials and Methods

Patients with atrial fibrillation who underwent an echocardiographic examination from January 1980 to December 1983 were identified. The period of time from the individual patient's echocardiogram to December 1985 was considered the total period of this study. A diagnosis of atrial fibrillation was accepted only if electrocardiographic evidence (6) or a physician's interpretation of an electrocardiogram could be obtained from the patient charts. Patients with a clinical history of mitral stenosis were excluded as were patients with echocardiographic evidence of mitral stenosis. The clinical, surgical, pathological and laboratory records were reviewed for the following information: age, sex, duration of atrial fibrillation, duration of clinical follow-up after onset of atrial fibrillation, echocardiographic determination of left atrial chamber size (11), evidence of valvular disease (aortic stenosis, aortic insufficiency, mitral regurgitation) (11), presence of coronary heart disease, congestive heart failure, cardiomyopathy, diabetes mellitus, hyperthyroidism, history of anticoagulation with wafarin, heparin, or antiplatelet agents (Persantine and/or aspirin), history of tobacco or alcohol use during period of study. In addition, charts were reviewed for evidence of systemic arterial embolic events. (See the example of the 3 page data collection form used for each patient, Fig. 4). In addition left atrial chamber size was determined by echocardiography in each patient. Of the 296 cases compiled, an attempt to establish clinical follow-up with each patient was made. The follow-up consisted of a form letter mailed to the patient's last known address followed by

a phone call to determine if a systemic embolism had occurred. The letter informed the patient of the study and alerted the patient that a follow-up phone call should be expected. During the phone conversation, the patient was asked about the use of anticoagulants, antiplatelet agents, additional hospitalizations since the time of echocardiogram and presence of symptoms consistent with an arterial embolic event. (See the example of the one page patient letter and one page questionnaire, Fig. 2 and Fig. 3, respectively). A total of 120 patients were excluded from the 296 for the following reasons:

| | |
|---|---|
| 96 patients | No follow-up obtainable because of death from unknown causes, patient unavailable, or unwilling to provide information. |
| 19 patients | Simultaneous presentation of an arterial embolic event and atrial fibrillation |
| 4 patients | Had prosthetic valve replacements prior to or during study. |
| 1 patient | Had peri-operative embolic event during cardiac surgery and atrial fibrillation could not be documented prior to surgery. |

TOTAL 120 patients excluded

The final number of confirmed cases of patients having atrial fibrillation without mitral stenosis with adequate follow-up reviewed in this study was 176.

Onset of Atrial Fibrillation:

The onset of atrial fibrillation was defined as the first electrocardiographic evidence of atrial fibrillation present in the patient chart or first documentation of atrial fibrillation by an attending physician in the medical records. Patients found to be in atrial fibrillation for the first time when hospitalized for an embolic event were excluded because it could not be determined whether atrial fibrillation preceeded the embolic event.

Chronic vs Paroxsysmal Atrial Fibrillation:

A separation between chronic and paroxysmal atrial fibrillation was made in this study. Paroxysmal atrial fibrillation was defined as patients whose medical records showed at least one spontaneous episode of normal sinus rhythm after onset of atrial fibrillation during the length of this study. Chronic atrial fibrillation was defined as patients with no documentation of spontaneous normal sinus rhythm after the onset of atrial fibrillation with at least 2 electrocardiograms more than one month apart. Undetermined type of atrial fibrillation was defined as patients with only 1 electrocardiogram in their medical records or less than one month between two consecutive electrocardiograms without spontaneous normal sinus rhythm.

Definition of Arterial Embolic Event:

Cases were reviewed for presentations of clinical emboli which were consistent with systemic arterial embolization. Embolic events were subdivided into 3 categories: central nervous system, mesenteric and peripheral events. In addition, embolic events were categorized according to correlation of clinical findings with laboratory findings. The arterial embolic event was considered to be definite if CT scan, angiographic or pathologic confirmation was available. A probable arterial embolic event lacked CT scan, angiographic and pathologic confirmation but clearly demonstrated physical neurologic deficits consistent with a cerebral vascular accident. A possible arterial embolic event was defined as a transient ischemic attack in the absence of carotid artery disease.

a. Cerebral vascular accident based on clinical diagnosis with CT scan confirmation = Definite.
b. Cerebral vascular accident based on clinical diagnosis without CT scan confirmation = Probable.
c. Transient ischemic attack in the absence of carotid artery disease defined by absence of carotid bruits on physical examination = Possible.
d. Onset of painful/numb extremity and/or loss of pulse with or without angiographic evidence of embolization resulting in embolectomy = Definite.
e. Clinical findings of mesenteric ischemia or infarction with angiographic confirmation of embolization; liver, splenic or renal infarction documented by liver/spleen scan or renal angiography = Definite (27).

Embolic events occurring before the echocardiogram were not included unless the patient experience a second event after the echocardiogram. Pulmonary embolisms were not included in this study.

Echocardiographic Evaluation:

Echocardiographic examinations were performed in a routine fashion with 2-D and M-Mode studies obtained in each patient. Left atrial chamber size was determined from the M-Mode study on each patient.

Definition of Cardiac Disease:

Non-Mitral Stenosis Valvular Disease:

In this study we excluded patients with clinical evidence of mitral stenosis. Patients with the following valvular lesions identified by clinical assessment including echocardiogram were included: aortic stenosis, aortic insufficiency and mitral regurgitation.

Coronary Heart Disease:

Patients with a clinical history of ischemic cardiomyopathy, angina and/or myocardial infarction confirmed by electrocardiographic findings were included in this grouping. One patient had a left ventricular aneurysm detected by echocardiogaphy.

Other Heart Disease:

This group included patients with nonischemic cardiomyopathy with ejection fraction <45%, hypertrophic cardiomyopathy, congenital heart disease, mitral valve prolapse, Sick-Sinus Syndrome and Wolff-Parkinson-White Syndrome.

No Cardiac Disease:

Patients without any of the above mentioned cardiac abnormalities were included in this group.

Underlying Clinical Conditions:

Patient charts were screened for presence of the following clinical conditions: angina, myocardial infarction, hypertension, hyperthyroidism, congestive heart failure and diabetes mellitus. A clinical history, laboratory values and/or x-ray studies were used to establish the presence of these clinical processes.

History of Anticoagulation Therapy:

Patients were considered to be anticoagulated if they were on an anticoagulant for greater than one month with therapeutic prothrombin times (1.5 times the control). In 4 patients the prothrombin times were not available but the patient stated that they were being followed by a physician and were told that their dose of anticoagulant was adequate.

Statistical Methods of Analysis:

The two-tailed test of significance and the nonparametric chi-square test were employed to determine the statistical significance for this study population.

# RESULTS

## Systemic Embolism:

The overall frequency of systemic arterial embolic events in patients having atrial fibrillation without mitral stenosis was 29/176 (17%). (See TABLE 1). Of the 29 arterial embolic events, 12/29 (41%) were definite, 14/29 (48%) probable and 3/29 ( 10%) were possible embolic events according to the criteria of CT scan confirmation, pathologic confirmation or embolectomy outlined in the methods. Of the total number of systemic arterial embolic events 24/29 (83%) involved the brain, 4/29 (14%) were peripheral and 1/29 (3%) was a mesenteric ischemic event.

The study population was divided into 4 groups to assess the frequency of embolic events according to type and extent of underlying heart disease: valvular disease (excluding mitral stenosis), coronary heart disease (ischemic cardiomyopathy, angina and/or myocardial infarction), other heart disease (hypertrophic cardiomyopathy, nonischemic cardiomyopathy, congenital heart disease, mitral valve prolapse, Sick-Sinus Syndrome and Wolff-Parkinson-White Syndrome), and combined heart diseases. (See TABLE 2). In patients with only valvular heart disease 2/10 (20%) embolized, only coronary heart disease 10/65 (15%) embolized, only "other" heart disease 2/10 (20%) embolized and with combined heart diseases 7/13 (54%) embolized. There was no significant difference between the embolic frequency of patients with only valvular heart disease, coronary heart disease or "other" heart disease. However, the presence or absence of any of the defined heart diseases was found to have a significant impact on embolic frequency.

Twenty-one of ninety-eight (21%) patients with underlying heart disease embolized as compared to 8/78 (10%) of those without heart disease ($P < .05$).

Duration of Atrial Fibrillation:

The mean length of time from echo to embolic event was 7 months (0 months - 45 months). The patients without emboli were followed for a mean of 35 months (0 days-71 months) from the time of echocardiography. The mean duration of atrial fibrillation from onset to the end of follow-up was 28 months (2 days-108 months) and 45 months (1 week - 228 months) in the embolic and nonembolic groups, respectively. Of the 29 patients with embolic events, 4 (14%) had the event within 1 week of the onset of atrial fibrillation, 4 (14%) from 2-4 weeks after the onset of atrial fibrillation, 1 (3%) from 2-6 months, 10 (35%) from 7-24 months and 10 (35%) from 3-9 years after the onset of atrial fibrillation. (See Figure 5).

Chronic vs Paroxysmal Atrial Fibrillation:

The type of atrial fibrillation as defined in the methods section proved to be an important influence on the frequency of embolic events. Twelve of forty-one (29%) patients with chronic atrial fibrillation embolized as compared to 13/104 (13%) of patients with paroxysmal atrial fibrillation. The difference between the frequencies was significant with $P < .02$.

Underlying Clinical Conditions:

The frequency of embolic events was similar in males and females. The mean age of the embolic group was 75 years ± 8.38 years as compared to the mean age of the nonembolic group which was 70 years ± 13.29 years (P=.0346). Four underlying clinical conditions were examined for their possible influence on the frequency of embolic events. Twelve of seventy-three (16%) patients with congestive heart failure (CHF) embolized compared to 17/103 (17%) patients without congestive heart failure (P=NS). Eighteen of twenty-four (21%) patients with hypertension (HTN) embolized compared to 11/92 (12%) patients without hypertension (P=NS). Eight of thirty-one (26%) patients with diabetes mellitus embolized versus 21/145 (15%) of patients without diabetes mellitus (P=NS). Four of seventeen (24%) patients with hyperthyroidism embolized versus 25/159 (16%) of patients without hyperthyroidism (P=NS).

Left Atrial Chamber Size:

The left atrial chamber sizes of the study population were divided into 2 groups: chamber size greater than or equal to 4.0cm and less than 4.0cm. A left atrial chamber size of 4.0cm or greater was chosen to separate this population for analysis because 4.0cm exceeds the upper limits of normal. Left atrial chamber size of greater than or equal to 4.0cm proved to be a very significant risk factor for embolization. Twenty-five of one-hundred and sixteen (22%) patients with left atrial chamber size greater than or equal to 4.0cm embolized compared to 4/60 (7%) patients with left atrial chamber size less than 4.0cm (P=.01). Thus, patients with left atrial chamber size greater than or equal to 4.0cm had 3 times the risk of embolization when compared to patients with left atrial chamber size less than 4.0cm. The mean left atrial

chamber size of the embolic group was 4.40cm ± .54cm. The mean left atrial chamber size of the nonembolic group was 4.14cm ± 1.03cm (P=NS). (See Figure 1).

Anticoagulation Status:

During the follow-up process it was determined that five of one hundred and seventy-six (3%) patients were chronically anticoagulated for more than 2 years. In none of these patients did an embolic event occur. Among the anticoagulated patients, the left atrial chamber size did not differ from the remaining nonembolic patients. Twenty-seven of twenty-nine (93%) patients were anticoagulated or treated with antiplatelet agents after the embolic event occurred. In this study patients were not analyzed for frequency of recurrent embolic events.

# DISCUSSION

Atrial fibrillation is an idiopathic entity as well as a complication of a variety of underlying cardiac diseases. Atrial fibrillation is seen in cardiac disease states such as Sick-Sinus Syndrome, Wolff-Parkinson-White Syndrome, pericarditis, rheumatic heart disease, coronary heart disease, mitral regurgitation, idiopathic dilated cardiomyopathy hypertrophic and infiltrative cardiomyopathies. In addition, atrial fibrillation is often seen in isolation with no known cause.

Unfortunately, atrial fibrillation has been associated with systemic embolization. Therefore, a variety of investigators have attempted to identify different clinical entities which increase a patient's risk of embolization when associated with atrial fibrillation. Thusfar, the literature has identified the following clinical entities: mitral stenosis/rheumatic heart disease, ischemic heart disease, hypertrophic cardiomyopathy and thyrotoxicosis.

Mitral stenosis and rheumatic heart disease have long been shown to increase the embolic frequency in patients with atrial fibrillation. In 1951, Daley reported the presence of mitral valve disease in 97% and atrial fibrillation in 90% of his patients who experienced a systemic embolism (16). Szekely's series in 1964 identified mitral stenosis as a risk factor for embolization by reporting a seven-times higher incidence of embolization in patients with chronic rheumatic heart disease and atrial fibrillation, than patients with chronic rheumatic heart disease in normal sinus rhythm (14). An autopsy series by Aberg in 1969 reported an embolic frequency of 53.5% in patients with atrial fibrillation and valvular (including mitral stenosis) or congenital

heart disease. He also reported an embolic frequency of 54.3% in patients with atrial fibrillation and valvular disease combined with ischemic heart disease (5). In 1976, Henry et al also identified mitral stenosis as a risk factor for embolization but, reported a much lower frequency of embolization. Twenty-six percent (22/85) of his study population with mitral valve disease experienced a systemic embolic event (8). In 1977, Hinton's autopsy series reported a 41% (29/70) embolic frequency in patients with atrial fibrillation and mitral valve disease (2). In 1978, results of a study by Neilson et al paralleled Henry's findings showing a 16.6% (37/234) embolic frequency among patients with mitral stenosis (4). The Framingham Study further supported these findings by reporting a seventeen fold increase in incidence of stroke among patients with chronic atrial fibrillation and rheumatic heart disease (8). Additionally, The Framingham Study reported that the presence of chronic atrial fibrillation alone placed patients at a five times greater risk for stroke than patients in normal sinus rhythm.

Originally, ischemic heart disease was not considered to increase the risk of embolization in patients with atrial fibrillation. Early autopsy studies by Beer and Ghitman in 1961 reported only a 2% (1/50) incidence of embolization in patients with atrial fibrillation and ischemic heart disease (7). However, Aberg's study in 1969 contradicted this finding. Aberg reported a higher frequency of embolization in patients with atrial fibrillation and valvular disease and ischemic heart disease (5). In 1977, Hinton et al divided patients into groups having atrial fibrillation with mitral valve disease and atrial fibrillation with ischemic heart disease. Hinton reported a 35% (59/171) incidence of embolization in patients with atrial fibrillation and ischemic heart disease (2). With the separation of atrial

fibrillation and ischemic heart disease from valvular disease, a risk of embolization comparable to that seen in mitral stenosis could be made. Consequently, recommendations for anticoagulation of this group were made.

Although rare, hypertrophic cardiomyopathy has also been identified as a risk factor which increases the embolic frequency in patients with atrial fibrillation. Henry et al reported a 25% (8/32) embolic frequency among patients with atrial fibrillation and asymmetric septal hypertrophy.

More recently, thyrotoxicosis has been associated with an increased embolic frequency among patients with atrial fibrillation. In 1980, Bar-Sela et al reported a 40% (12/30) embolic frequency in patients with thyrotoxicosis and atrial fibrillation (19). None of the patients with thyrotoxicosis without atrial fibrillation embolized (0/112). However, the authors note that the patients with atrial fibrillation had a higher prevalence of rheumatic and hypertensive heart disease (19), of which rheumatic heart disease is known to be an independent risk factor for embolization.

In the majority of the studies discussed, no separation or comparison between chronic and paroxysmal atrial fibrillation was made. The Framingham Study included only patients with chronic atrial fibrillation as defined by the presence of atrial fibrillation on biennial examination (8). Daley et al report that the majority of embolic events in their study occur in chronic atrial fibrillation versus paroxysmal atrial fibrillation but the definition of chronic and paroxysmal atrial fibrillation is unclear (16). Henry et al report that 91% of their embolic events occur in chronic atrial fibrillation which they define as atrial fibrillation present at the time of echocardiogram

or if in sinus rhythm at the time of echocardiogram had a history of atrial fibrillation lasting more than 24 hours requiring cardioversion (3). Reports by Beer and Ghitman, Szekely, Aberg, Hinton et al, Neilson et al and Bar-Sela do not distinguish between the two types of atrial fibrillation.

Despite other findings presented in the literature, it is still generally accepted that only the combination of atrial fibrillation and mitral stenosis poses a great enough risk of embolization to warrant long-term anticoagulation therapy and its complications. The present study sets out to identify whether left atrial chamber size can be used as a prognosticator of embolic risk in patients with atrial fibrillation without mitral stenosis.

Systemic Embolism:

An attempt was made to subdivide systemic emboli into definite, probable and possible according to laboratory information available to correlate the clinical diagnosis. Since the thrust of this study was to assess the influence of left atrial size on embolic frequency, the mean left atrial chamber sizes of the three subgroups were compared (P=NS). Therefore it was assumed for the remainder of this study, that all embolic events were correctly diagnosed regardless of ability to correlate the clinical diagnosis with laboratory findings. Thusfar, the distinction between embolic and thrombotic cerebral vascular accidents has been at best difficult, in all but autopsy reviews (17). Like Wolf et al in The Framingham Study, all strokes and transient ischemic attacks are considered embolic in this study (8). The overall frequency of systemic embolization in patients with atrial fibrillation without mitral stenosis was 29/176 (17%). Eighty-three percent were cerebral

embolic events which is comparable to the previously reported frequency of cerebral emboli among patients with embolic events (5).

Underlying Clinical Conditions:

The presence of any underlying cardiac abnormality made a significant impact on embolic frequency in the study population. The presence of isolated non-mitral stenosis valvular disease or coronary heart disease did not significantly increase the embolic frequency in this study. These findings contrast reports by Aberg, Coulshed and Hinton of an increase embolic frequency in patients with valvular heart disease or congenital heart disease combined with atrial fibrillation. However, patients with the presence of any of the defined heart diseases in this study had an increased embolic frequency as compared to patients with no heart disease, 21/98 (21%) versus 8/78 (10%), respectively ($P < .05$). Multivariant analysis was not performed in this study. Therefore the effect of two or more underlying cardiac diseases on the embolic frequency could not be assessed.

Chronic vs Paroxsysmal Atrial Fibrillation:

This study also shows that chronic atrial fibrillation is associated with and increased frequency of embolization. Twenty-nine percent of patients with chronic atrial fibrillaiton embolized versus 13% of patients with paroxysmal atrial fibrillation ($P < .02$). Henry et al reported that 91% (20/22) of their embolic events occurred in patients with chronic atrial fibrillation (3). Daley supports these findings with his report that the majority of embolic events occurred during chronic atrial fibrillation. The Framingham Study only included patients with chronic atrial fibrillation. Few studies have attempted

to distinquish between paroxysmal and chronic atrial fibrillation. This may be due to the difficulty of distinquishing between the presence of paroxysmal or chronic atrial fibrillation without longterm cardiac monitoring. In this study chronic atrial fibrillation was defined by the absence of documented spontaneous sinus rhythm on two separate electrocardiograms one month or more apart. Patients who were chemically or electrically cardioverted were included in this group. In addition, it appears that not only the type of atrial fibrillation but the timing of the embolic event may have implications for recommendations of anticoagulation therapy. Other researchers have proposed that embolic events are most likely to occur in the first one month to six months of atrial fibrillation (3). The Framingham Study failed to identify such a vunerable period in their review. Although the present study reports that 28% of embolic events occurred within one month onset of atrial fibrillation, an additional 38% occur between 1 month and 24 months. A total of 66% of the embolic events occurred within 2 years of onset of atrial fibrillation. Thus, when indicated, anticoagulation therapy while important at the onset of atrial fibrillation may be of benifit to patients found to be in atrial fibrillation of longer duration.

Age:

The incidence of embolization was found to increase among patients with increased age in this study population. The embolic group had a mean age of 75 years $\pm$ 8 years compared to the nonembolic group mean of 70 years $\pm$ 13 years (P=.03). Coulshed and others have previously reported an increased incidence of systemic embolization in persons with

increased age (15).

As detailed earlier, the identification of subgroups of patients at risk for embolization with atrial fibrillation and other clinical entites have rarely resulted in the widespread use of anticoagulation therapy, except in the case of mitral stenosis. The results of this study also identify subgroups of patients at risk for embolization: patients with underlying organic heart disease, chronic atrial fibrillation and increased age. However, the most important finding in this study relates to left atrial chamber size and its ability to predict patients at risk for systemic embolization.

Influence of Left Atrial Chamber Size:

This series shows that a left atrial chamber size of 4.0cm or more is a very significant risk factor in patients having atrial fibrillation without mitral stenosis. The left atrial chamber measurements obtained in the usual fashion using 2-D and M-mode echocardiography revealed that 25/116 (22%) patients with left atrial chamber size greater than or equal to 4.0cm experienced a systemic arterial embolic event. Four of sixty (7%) patients with left atrial chamber size less than 4.0cm embolized (P=.0124). These results show that a patient with atrial fibrillation without mitral stenosis with left atrial size greater than or equal to 4.0cm is at 3 times greater risk for embolization than a patient with left atrial size less than 4.0cm. Left atrial chamber size was determined on an average of 7 months (0 - 45 months) prior to embolization. Whether left atrial chamber size changes rapidly or significantly in the absence of mitral stenosis remains undetermined.

A recently published abstract by D'Cruz et al reports that left atrial dimensions determined by echocardiography were found to be significantly larger in their embolic population. Ninety percent of the embolic group had enlarged left atrial size versus 20% of the nonembolic group. However, their study population was identified by the presence of a stroke. In their study population neither the onset of atrial fibrillation nor the type of atrial fibrillation was known.

None of the embolic events occurred in patients on therapeutic anticoagulation demonstrated by prothrombin times in the therapeutic range (1.5 times control). Patients who experienced embolic events were not followed after their initial embolic event to assess the frequency of recurrent embolic episodes. The relative risk of embolization does not increase as left atrial size increases suggesting a threshold effect takes place near a chamber size of 4.0cm. The embolic group did not have many patients with left atrial chamber size greater than 5.0cm. Therefore, the number of patients did not lend itself to rigorous statistical analysis to challenge this possibility.

One major bias in this study is the identification of patients with atrial fibrillation from a predominantly hospitalized population. Ninety-six percent of the patients in this study had the initial echocardiogram done as inpatients. This may have selected for patients with less ability to tolerate atrial fibrillation causing them to seek medical attention for symptomatology. Once these patients were identified in an inpatient setting, echocardiography could be easily obtained. Conversely, patients who are asymptomatic and find out they have atrial fibrillation on routine electrocardiogram may be less likely to have echocardiography recommended as part of their work-up.

Conclusions:

Among patients with atrial fibrillation without mitral stenosis the following conclusions are drawn:

1. Patients with left atrial chamber size greater than or equal to 4.0cm are significantly more likely to embolize than patients with left atrial chamber size less than 4.0cm.
2. Patients with underlying organic heart disease compared to those without underlying organic heart disease are more likely to embolize.
3. Patients with chronic atrial fibrillation are more likely to embolize than those patients with paroxysmal atrial fibrillation.
4. The risk of embolization is not confined to any discrete time period after the onset of atrial fibrillation.

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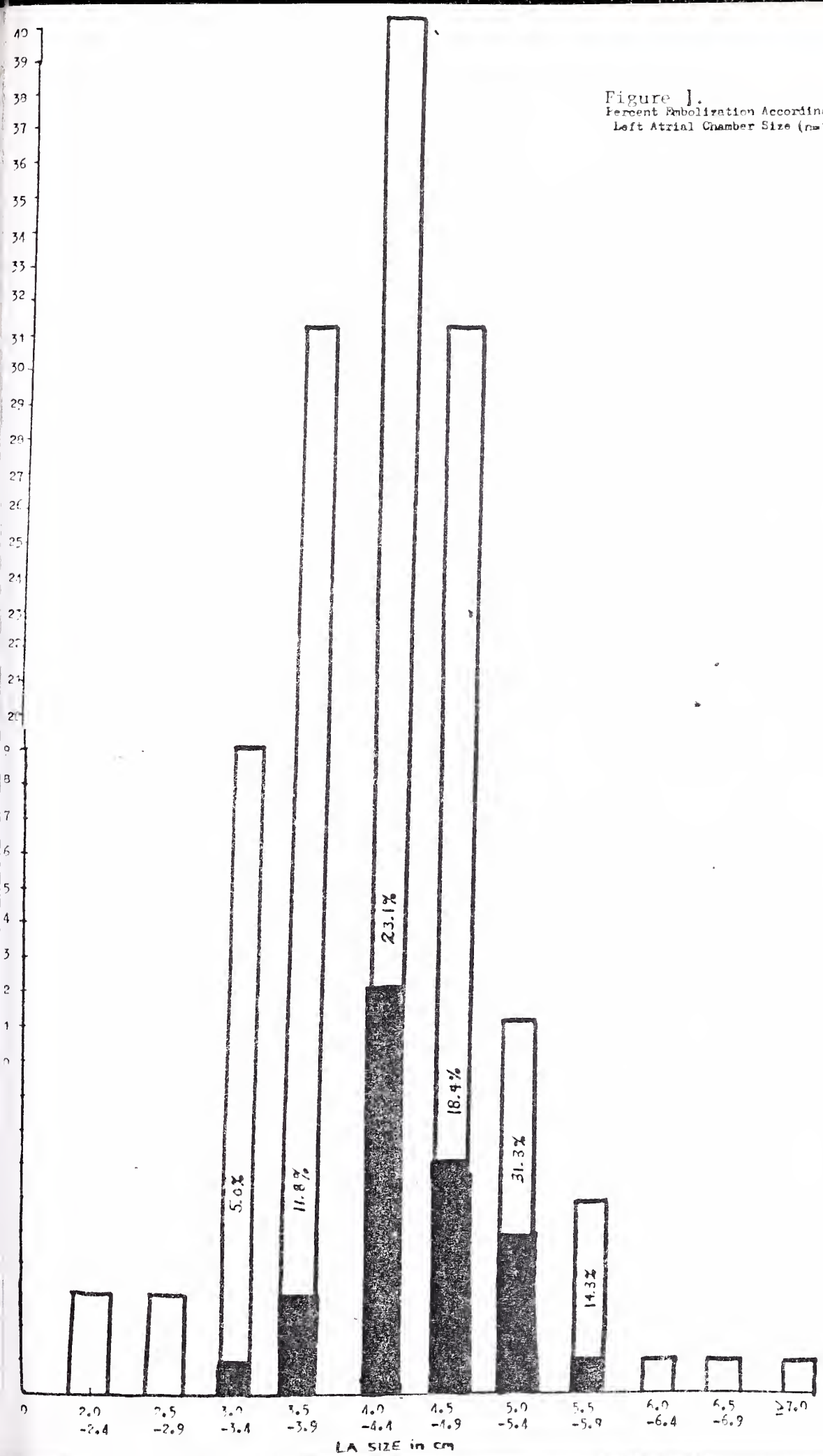
Figure 1.
Percent Embolization According to Left Atrial Chamber Size (n=176)



Legend

Figure 1

The blackened portion of the bar graph shows the percent of patients with a given left atrial chamber size that embolize. No patients with left atrial chamber sizes less than 3.0cm or greater than 6.0cm experienced and embolic event.

Figure 2.

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January 24, 1986

Bessie Philopence
25 Gordon Court
New London, CT 06320

Dear Mrs. Philopence:

We are currently studying patients with an irregular heart beat who have undergone an echocardiogram during 1980-1983 at Yale-New Haven Hospital. At some point during this time period, your physician requested than an echocardiogram (a test to evaluate the heart's chambers and valves) be performed. In the next several weeks, a member of our research staff will be contacting you by telephone to ask you a few questions. These questions will pertain to your present state of health and medications you have been taking since you had an echocardiogram. The information gathered will not change your present therapeutic regimen in any way. The information gathered from you will be combined with information from other patients with irregular heart beats. Please be assured that all information will remain confidential and that you will not be identified by name in any reports of publications resulting from this study.

We would appreciate your help in answering these questions which will only take approximately 10 minutes of your time and can be done on the telephone. Your participation is voluntary and you may refuse to participate or answer any particular questions without affecting future relationships with physicians at Yale-New Haven Medical Center. Please feel free to ask any questions during our conversation.

Thank you in advance for your cooperation.

Sincerely,

Henry S. Cabin

Henry S. Cabin, M.D. F.A.C.C.

Cynthia Hall

Cynthia Hall, Medical Student
Yale University School of Medicine

Figure 3.

PATIENT QUESTIONNAIRE

Hi, my name is Cynthia Hall and I'm calling from Yale-New Haven Hospital. You received a letter a few weeks ago informing you of a study which I am conducting in conjunction with the Cardiology Department at Yale. You have already undergone an echocardiogram to assess the size and function of your heart and its valves. I would like to just take a few minutes to ask ask you a few questions pertaining to your health and medications since this test was performed. Your participation in this study is voluntary and you may refuse to answer any or all questions, if you wish. Would you like to take about 10mins now to answer a few questions?

1. Have there been any changes in your medications since your echocardiogram?

2. Have you started taking any new medications?

3. Are you taking Warfarin(Coumadin), Persantine or aspirin regularly to thin your blood?

4. How much and how often?

5. Have you required any hospitalizations since your echocardiogram?

6. If so, what for? when? where?

7. Who was your physician during these hospitalizations?

8. Did you have any special studies like CT scan, Liver/Spleen scan, Renal scan or dye studies?

9. Have you experienced a painful or numb extremity that has required medical attention?

10. Have you experienced any difficulties with your speech, vision, movement or sensation of any part of your body?

Thank you very much for your cooperation with this study. Are there any questions you would like to ask me at this time? Thank you and goodbye

Atrial Fibrillation/Systemic Embolization Study Figure 4

I. Personal Background

Name_____ Date of Birth_____ Sex_____

Address_____

Unit Number_____ Phone Number_____ Attending_____

Date of Death_____ Cause_____

II. Echo Data

Date_____ Reason_____

LA Size_____

Other Echo Findings_____

III. Other Medical Problems

| | |
|---|---|
| HTN | CHF |
| Tobacco | RHD AoV___ MV___ Prosthesis___ |
| EtOH | Coronary Heart Disease |
| Hyperthyroidism | MI Date_____ |

IV. Laboratory Tests and Interpretations

Index ECG Date_____

| | |
|---|---|
| LA Enlargement | Other Arrhythmias |
| LVH | MUGA Scan |
| MI | Index Chest X-Ray |

V. Medical Management of Arrhythmias

| | |
|---|---|
| DC Cardioversion | Inpatient Anticoagulation |
| Chemical Cardioversion | Outpatient Anticoagulation |
| Antiarrhythmics | Beginning of Outpatient Anticoagulation |
| | type_____ |

VI. Prothrombin Time Data

PT less than 1.5 time control

PT greater than or equal to 1.5-2 times control

VII. Atrial Fibrillation History

| Date of ECG | Therapy | Drugs | A. Fib. | NSR | Other |
|---|---|---|---|---|---|

VII. Symptoms and/or Documentation of Embolization

CNS Date of Embolization_____

CT Scan Findings_____

Angiogram Findings_____

Autopsy Findings_____

Clinical Findings on Physical Examination_____

_____

presence of absence of carotid artery disease_____

BOWEL Date of Embolization_____

Pain Symptoms_____

Angiogram Findings_____

Autopsy Findings_____

Clinical Findings_____

OTHER ABDOMINAL FINDINGS Date of Embolization_____

Liver Infarction/Splenic Infarction/Kidney Infarction

Liver/Spleen Scan Findings_____

EXTREMITY

Pain

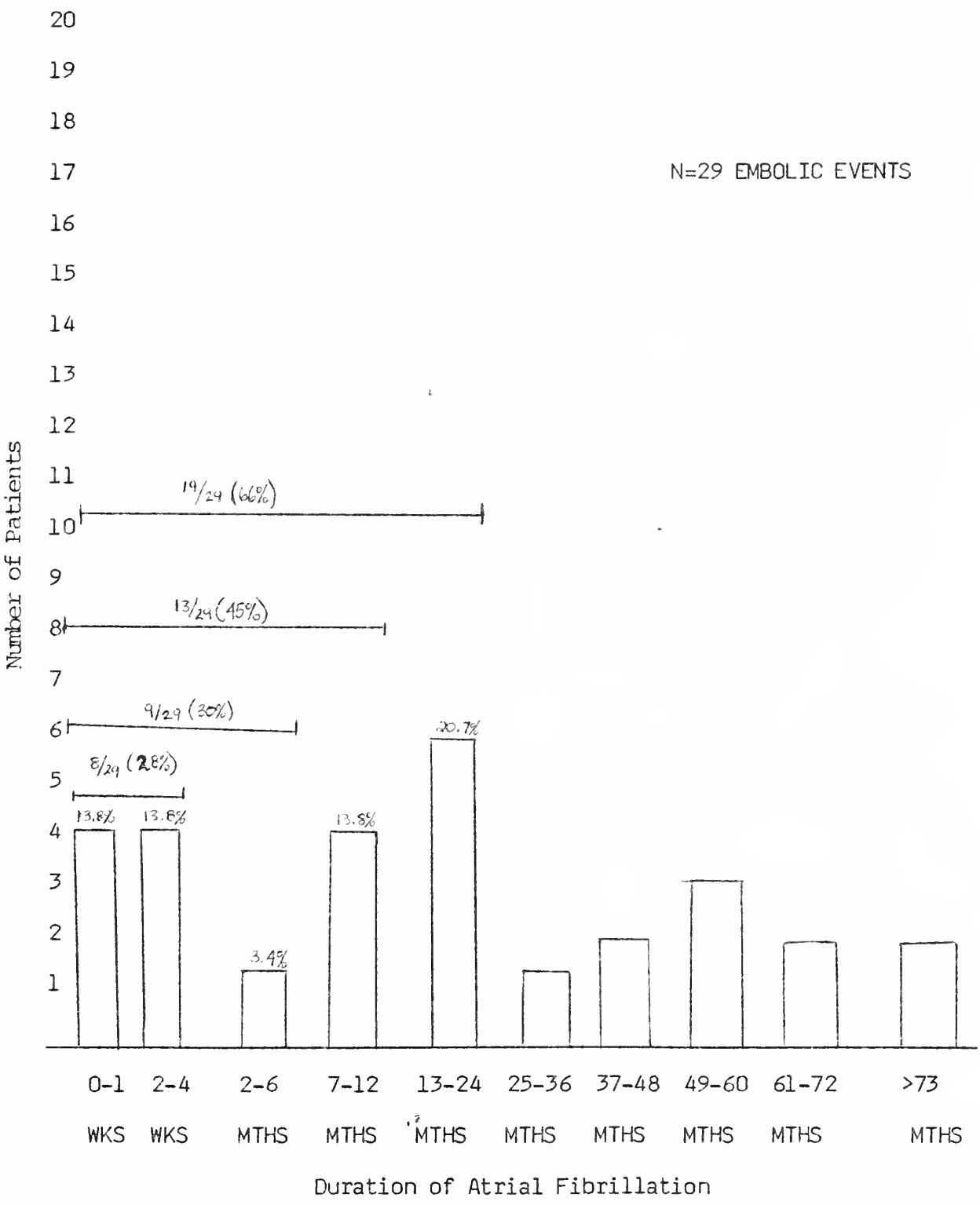
Loss of Pulse

Angiogram Findings

Embolectomy Yes/No

Figure 5

TIMING OF EMBOLIC EVENT AFTER ONSET OF ATRIAL FIBRILLATION



Legend

Figure 5

This figure shows the distribution of embolic events according to duration of atrial fibrillation. Twenty-eight percent of the embolic events occur within one month of onset of atrial fibrillation, 17% between 2 months and 12 months and 21% between 1 year and 2 years. This shows that the risk of embolization exist far longer than the 1-6 month period of vunerability described by other authors (See Discussion).

TABLE 1

EMBOLIC VS. NONEMBOLIC GROUP

| | EMBOLIC n=29 | NONEMBOLIC n=147 |
|---|---|---|
| AGE | Mean 75YRS±8YRS | Mean 70YRS±13YRS |
| SEX F | 14(48%) | 67(46%) |
| M | 15(52%) | 80(54%) |
| CHF | 12(41%) | 60(41%) |
| HTN | 18(62%) | 63(43%) |
| DIABETES | 8(28%) | 23(16%) |
| THYROID | 4(14%) | 13(9%) |
| CHD | 17(59%) | 61(42%) |
| VALVE DX | 7(24%) | 11(8%) |
| "OTHER"HD | 4(14%) | 18(12%) |
| NO HD | 18(62%) | 118(80%) |
| CHRONIC AF | 12(41%) | 29(20%) |
| PAROXY AF | 13(45%) | 91(62%) |
| UNDETERM AF | 4(14%) | 27(18%) |
| DURATION OF AF | Mean 28mths (2days-108mths) | Mean 46mths (1wk-228mths) |
| MTHS F/U | 7mths (0-45mths) | 35mths (0days-71mths) |
| % EMBOLIZATION | | |
| OF CHRONIC | 12/41(29%) | 0 |
| PAROXY | 13/104(13%) | 0 |
| UNDETERM | 4/31(13%) | 0 |
| MEAN LA SIZE | 4.40CM±.54CM | 4.16CM±1.03CM |

TABLE 2

ORGANIC CARDIAC ABNORMALITIES

| | NON-MITRAL STENOSIS VALVE DX n=10 | CORONARY HEART DISEASE n=65 | "OTHER" HEART DISEASE n=10 | COMBINED HEART DISEASE n=13 | NO HEART DISEASE n=78 | TOTAL n=176 |
|---|---|---|---|---|---|---|
| AGE | - | - | - | - | - | 71±13yrs |
| SEX F | 6(60%) | 22(34%) | 5(50%) | 6(50%) | 42(54%) | 81(46%) |
| M | 4(40%) | 43(66%) | 5(50%) | 7(54%) | 36(46%) | 95(54%) |
| CHF | 4(40%) | 36(55%) | 7(70%) | 6(46%) | 19(24%) | 72(40%) |
| HTN | 6(60%) | 33(50%) | 5(50%) | 6(46%) | 31(40%) | 81(46%) |
| DIABETES | 0 | 19(29%) | 1(10%) | 2(46%) | 9(12%) | 31(18%) |
| HYPER-THYROID | 1(10%) | 8(12%) | 0 | 0 | 8(10%) | 17(10%) |
| CHRONIC AF | 5(50%) | 19(29%) | 2(20%) | 7( 54%) | 8(10%) | 41(23%) |
| PAROXY AF | 3(30%) | 37(57%) | 4(40%) | 5(39%) | 55(71%) | 104(59%) |
| UNDETERM AF | 2(20%) | 9(14%) | 4(40%) | 1(8%) | 15(19%) | 31(18%) |
| PERCENT EMBOLIZATION | | | | | | |
| OF CHRONIC | 2/5(40%) | 4/19(21%) | 0/2 | 3/7(43%) | 3/8 (37%) | 12/41(29%) |
| PAROXY. | 0/3 | 5/37(14%) | 1/4(25%) | 4/5(80%) | 3/55(6%) | 13/104(13% |
| UNDETERM | 0/2 | 1/9(11%) | 1/4(25%) | 0/1 | 2/15(13%) | 4/31(13%) |
| EMBOLIC | 2(20%) | 10(15%) | 2(20%) | 7(54%) | 8(10% ) | 29(17%) |
| NONEMBOLIC | 8(80%) | 55(87%) | 8(80%) | 6(46%) | 70(90%) | 147(84%) |

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